

by the DNA sequence to be examined or a limited number of different ribonucleic acids and peptides encoded by DNA sequences to be examined,

- (c) screening said transduced cells to see whether some of them have altered a preselected [phenotypic trait] cellular function, said screening being one which does not require knowledge of 1) chains of mechanisms in the cell, 2) enzymes in the cell, 3) signalling pathways in the cell, or 4) receptors in the cell which generate the preselected [phenotypic trait] cellular function, and
- (d) selecting and cloning cells which have altered the preselected [phenotypic trait] cellular function,

wherein the pool of appropriate vectors in step (a) contains synthetic totally [or partly] random DNA sequences [selected from the group consisting of:

- i) synthetic totally random DNA sequences;
- ii) synthetic random DNA sequences wherein stop codons are absent;
- iii) synthetic DNA sequences which encode random amino acid sequences with an even distribution of amino acids;
- iv) synthetic DNA sequences defined in (i), (ii), or (iii) separated by codons which enable specific post-translational modifications of all expressed peptides or which encode anchor residues;
- v) synthetic DNA sequences defined in (i), (ii), (iii), or (iv) coupled to coding sequences of purification tags in order to facilitate the purification and identification of expressed peptides; and
- vi) synthetic DNA sequences defined in (i), (ii), (iii), (iv), or (v) coupled to or inserted into the coding sequence of a protein];

and wherein

(e) the vector DNA in the [phenotypically altered] cells having altered cellular function is isolated and sequenced, and the sequences of the ribonucleic acids or peptides effecting alteration of the preselected [phenotypic trait] cellular function are deduced from the sequenced vector DNA;

and/or

(f) the ribonucleic acids or peptides effecting alteration of the preselected [phenotypic trait] cellular function are used directly for isolation and identification of a ligand molecule to said ribonucleic acids or peptides

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Claims 3 and 4, lines 1-3 of each claim, insert --random-- after "the synthetic" (each occurrence).

Claims 5, 8, 9, 14; and 22, line 2 of each claim, insert --synthetic-- before "random" (each occurrence).

Claim 5, line 5, and Claim 7, line 5, delete "or partly" before "random" (each occurrence).

Claim 11, line 3, insert --synthetic-- before "random".

Claim 26, line 2, and Claim 41, line 3, delete "phenotypic trait" and insert "cellular function".

Claim 30, line 2, insert --random-- after "synthetic".

Claim 31, line 1, insert --random-- after "synthetic".

Please cancel Claims 19, 32, 33, 43-47, 49-52, and 54-58 without prejudice.

42. (Twice Amended) A method for identification of biologically active ribonucleic acids or peptides or cellular ligands to the biologically active ribonucleic acids or peptides, which comprises the steps of

- (a) producing a pool of appropriate vectors each containing a DNA sequence to be examined,
- (b) efficiently transducing said vectors into a number of identical eukaryotic cells in such a way that each cell expresses either a single ribonucleic acid and possibly peptide encoded by the DNA sequence to be examined or a limited number of different ribonucleic acids and peptides encoded by DNA sequences to be examined,
- (c) screening said transduced cells to see whether some of them have up-regulated or down-regulated a preselected [biological effect] cellular function, and
- (d) selecting and cloning cells which have up-regulated or down-regulated the preselected [biological effect] cellular function,

wherein the pool of appropriate vectors in step (a) contains synthetic totally [or partly] random DNA sequences [selected from the group consisting of:

- i) synthetic totally random DNA sequences;
- ii) synthetic random DNA sequences wherein stop codons are absent;
- iii) synthetic DNA sequences which encode random amino acid sequences with an even distribution of amino acids;
- iv) synthetic DNA sequences defined in (i), (ii), or (iii) separated by codons which enable specific post-translational modifications of all expressed peptides or which encode anchor residues;

- v) synthetic DNA sequences defined in (i), (ii), (iii), or (iv) coupled to coding sequences of purification tags in order to facilitate the purification and identification of expressed peptides; and
- vi) synthetic DNA sequences defined in (i), (ii), (iii), (iv), or (v) coupled to or inserted into the coding sequence of a protein];

and wherein

- (e) the vector DNA in the selected and cloned cells is isolated and sequenced, and the sequences of the ribonucleic acids or peptides effecting up-regulation or down-regulation of the preselected [biological effect] cellular function are deduced from the sequenced vector DNA; and/or
- (f) the ribonucleic acids or peptides effecting up-regulation or down-regulation of the preselected [biological effect] cellular function are used directly for isolation and identification of a ligand molecule to said ribonucleic acids or peptides.

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Please add the following new claims:

--59. The method according to claim 1, wherein the synthetic random DNA sequences do not include stop codons.

60. The method according to claim 1, wherein the synthetic random DNA sequences encode random amino acid sequences with an even distribution of amino acids.

61. The method according to claim 1, wherein the synthetic random DNA sequences are separated by codons which enable specific post-translational modifications of all expressed peptides or which encode anchor residues.

62. The method according to claim 1, wherein the synthetic random DNA sequences are coupled to coding sequences of purification tags in order to facilitate the purification and identification of expressed peptides.

63. The method according to claim 1, wherein the synthetic random DNA sequences are coupled to or inserted into the coding sequence of a protein.

64. The method according to claim 42, wherein the synthetic random DNA sequences do not include stop codons.

65. The method according to claim 42, wherein the synthetic random DNA sequences encode random amino acid sequences with an even distribution of amino acids.

66. The method according to claim 42, wherein the synthetic random DNA sequences are separated by codons which enable specific post-translational modifications of all expressed peptides or which encode anchor residues.